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10/534,433	11/21/2005	Sang-Kyu Lee	NAMNP0103US	5833

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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,433	LEE ET AL.	
	Examiner	Art Unit	
	MICHELE K. JOIKE	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of species Sim-2 and intraperitoneal in the reply filed on March 7, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However, the species election is withdrawn.

Specification

The disclosure is objected to because of the following informalities: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences were set forth that lack sequence identifiers. These sequences include the sequences listed in the claims and throughout the specification. Nucleotide sequences with 10 or more nucleotides and amino acid sequences with 4 or more amino acids require sequence identifiers. If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP § 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP § 2422.02).

Page 3 contains an amino acid sequence with no sequence identifier.

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

Claim Objections

Claims 6 and 13 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 6 and 13 contain intended use language and do not further limit the binding complex of claims 1 and 2.

Claim 1 is objected to because of the following informalities: The full name for PTD (in line 2) should be used the first time, as PTD could mean something other than protein transduction domain. Appropriate correction is required.

Claims 1, 7 and 8 are objected to because of the following informalities: "DNA/RNA" should be "DNA or RNA" if that is what is intended. "DNA/RNA" can also be read to mean a DNA/RNA hybrid. Appropriate correction is required.

Claims 3 and 11 are objected to because of the following informalities: "MTS<" should be "MTS," in line 3. Appropriate correction is required.

Claim 8 is objected to because of the following informalities: In part iii, "NDA" should be "DNA". Appropriate correction is required.

Claim 10 is objected to because of the following informalities: The word "encoding" is duplicated in lines 2-3. Appropriate correction is required.

Claim 14 is objected to because of the following informalities: Claim 14 has the wrong status identifier. It is a new claim. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ye et al.

Applicants claims a binding complex for delivering DNA/RNA into the cytoplasm or nucleus, comprising a fusion protein of PTD (Tat, VP22 or ANTP) with one or more binding proteins having a DNA binding domain; a DNA binding sequence which is specifically bound to the DNA binding domain; and an inducible promoter expressing a gene specifically in specific species, tissues, organs or cells. The binding complex can also contain an NLS. Also claimed is a vector comprising DNA encoding a PTD, DNA encoding a binding protein and a promoter. The language "for delivering DNA/RNA into

cytoplasm or nucleus" in claim 1 is intended use language and is not given any weight. In claims 6 and 13, the wherein clause is also intended use language and is not given any patentable weight.

Applicants also claim a method for delivering a biological regulator into a cell, comprising steps: i) Preparing a peptide transducing recombinant expression vector which comprises DNA encoding a PTD, DNA encoding a binding protein having a DNA binding domain, and an expression regulatory sequence operatively bound to the vector; ii) Obtaining a fusion protein by expression of the vector of step i) in a host cell; iii) Obtaining a binding complex by binding of one or more biological regulators selected from the group consisting of the fusion protein of step ii), protein, DNA/RNA, fat, carbohydrate and chemicals by chemical or physical covalent or non-covalent bond; and iv) Mixed-culturing the binding complex of step iii) with cell cultures in vivo or ex vivo through routes including intramuscular, intraperitoneal, intravein, oral, nasal, subcutaneous, intradermal, mucosal or inhalation.

Ye et al (Phar. Res. 19(9): 1302-1309, 2002, specifically pp. 1302-1305, especially Fig. 1) teach a binding complex comprising a chimeric protein (protein fusion) comprising an HA epitope, a Gal4(DBD)-VP16 and a His tag. The chimeric protein can also include a Tat or VP22. Ye et al teach a vector (peptide transducing recombinant (PTD) expression vector) encoding the above complex, including a promoter, that is co-transformed with a reporter plasmid encoding a luciferase gene linked to five tandem repeats of the Gal4 binding site (inducible promoter) (p. 1304-05). The chimeric protein is produced, and the reporter plasmid binds to the chimeric protein completing the

binding complex. The binding complex is moved from the culture medium to the nucleus as evidenced by activation of the reporter gene (p. 1304). See specifically Fig. 1. The vector encoding the chimeric protein can also contain a sequence encoding a nuclear localization sequence (p. 1303). Since claims 6 and 13 are intended use claims, only the binding complex is required to meet the limitations of the claim. In regard to claims 4 and 12, the Gal4 promoter is a promoter that expresses a gene in different cell types, however, it inherently will express at different levels depending on the cell or species, etc..

Ye et al also teach a method for delivering the two vectors into HEK293 cells (Materials & Methods). The PTD vector is made as described above, and expression of the vector produces the chimeric protein in HEK293 cells. The binding complex is formed when the reporter plasmid (also made as described above) binds the chimeric protein. Co-culture assays are performed through adding cells to culture plates. Claim 7 has routes including intramuscular, intraperitoneal, intravein, oral, nasal, subcutaneous, intradermal, mucosal or inhalation. The Examiner is interpreting "including" as open language, which means that the list of routes is not exclusive, and adding cells to a plate for co-culturing is an acceptable route. Again, an NLS sequence can be added to the PTD vector.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-8, and 10-13 are rejected under 35 U.S.C. 102(e) as being anticipated by US 7,354,737.

The applied reference has a common assignee and inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Applicants claims a binding complex for delivering DNA/RNA into the cytoplasm or nucleus, comprising a fusion protein of PTD (Sim-2, Tat, ANTP, MTS) with a GAL4 DNA binding domain, and a His tag; a DNA binding sequence which is specifically bound to the DNA binding domain; and an inducible promoter expressing a gene specifically in specific species, tissues, organs or cells. Also claimed is a vector comprising DNA encoding a PTD, DNA encoding a binding protein and a promoter.

Applicants also claim a method for delivering a biological regulator into a cell, comprising steps: i) Preparing a peptide transducing recombinant expression vector which comprises DNA encoding a PTD, DNA encoding a binding protein having a DNA binding domain, and an expression regulatory sequence operatively bound to the

vector; ii) Obtaining a fusion protein by expression of the vector of step i) in a host cell; iii) Obtaining a binding complex by binding of one or more biological regulators selected from the group consisting of the fusion protein of step ii), protein, DNA/RNA, fat, carbohydrate and chemicals by chemical or physical covalent or non-covalent bond; and iv) Mixed-culturing the binding complex of step iii) with cell cultures in vivo or ex vivo through routes including intramuscular, intraperitoneal, intravein, oral, nasal, subcutaneous, intradermal, mucosal or inhalation.

US 7,354,737 (see entire patent, specifically columns 4-8) teaches a binding complex for delivering DNA/RNA into the cytoplasm or nucleus, comprising a fusion protein of PTD (Sim-2, Tat, ANTP, MTS) with one or more binding proteins having a DNA binding domain; a DNA binding sequence which is specifically bound to the DNA binding domain; and an inducible promoter expressing a gene specifically in specific species, tissues, organs or cells. Also claimed is a vector comprising DNA encoding a PTD, DNA encoding a binding protein and a promoter.

It also teaches a method for delivering a biological regulator into a cell, comprising steps: i) Preparing a peptide transducing recombinant expression vector which comprises DNA encoding a PTD, DNA encoding a binding protein having a DNA binding domain, and an expression regulatory sequence operatively bound to the vector; ii) Obtaining a fusion protein by expression of the vector of step i) in a host cell; iii) Obtaining a binding complex by binding of one or more biological regulators selected from the group consisting of the fusion protein of step ii), protein, DNA/RNA, fat, carbohydrate and chemicals by chemical or physical covalent or non-covalent bond;

and iv) Mixed-culturing the binding complex of step iii) with cell cultures in vivo or ex vivo through routes including intramuscular, intraperitoneal, intravein, oral, nasal, subcutaneous, intradermal, mucosal or inhalation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 9 and 14 are rejected under 35 U.S.C. 103(a) as being obvious over US 7,354,737 in view of Cartier et al.

The applied reference has a common assignee and inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a)

might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Applicant claims the binding complex containing a NLS sequence combined with the PTD.

US 7,354,737 teaches all of the limitations as described above. However, it does not teach a NLS sequence combined with the PTD.

Cartier et al (Gene Therapy 9: 157-167, 2002, specifically p. 157, 158) teach a synthetic peptide containing a NLS and are bound to DNA, so the resulting complex of the peptide, NLS and DNA can be transported into the nucleus.

The ordinary skilled artisan, desiring to use a NLS sequence combined with the PTD, would have been motivated to combine the teachings of US 7,354,737 teaching a a binding complex for delivering DNA/RNA into the cytoplasm or nucleus, comprising a fusion protein of PTD (Sim-2, Tat, ANTP, MTS) with one or more binding proteins having a DNA binding domain; a DNA binding sequence which is specifically bound to the DNA binding domain; and an inducible promoter expressing a gene specifically in specific species, tissues, organs or cells, with the teachings of Cartier et al teaching a synthetic peptide containing a NLS and are bound to DNA, so the resulting complex of the peptide, NLS and DNA can be transported into the nucleus because Cartier et al state that the transport of the therapeutic DNA from the cytoplasm into the nucleus is an inefficient process and is considered as the major limiting step in nondividing cells. Therefore, one of the strategies to improve nuclear uptake of DNA is to take advantage of the cellular nuclear import machinery. It would have been obvious to one of ordinary skill in the art to use a NLS sequence because Cartier et al teach a NLS can be useful in a drug delivery system. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K Joike, Ph.D./

Michele K Joike, Ph.D.
Examiner
Art Unit 1636